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REPORT OF THE 1992 AFOSR WORKSHOP ON THE FUTURE OF EEG AND MEG

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I. Introduction

A workshop on the prospects of the electroencephalogram (EEG) and the magnetoencephalogram (MEG) for elucidating human brain function was held at Virginia Beach, Virginia from May 17-22, 1992, and was attended by scientists and physicians from a variety of disciplines, as well as by Federal government officials. Planning for this had been initiated by Drs. Harold Weinstock and Alfred Fregly of the U.S. Air Force Office of Scientific Research in the spring of 1991, and the workshop was organized by the authors of this report.

The purpose of the workshop was to discuss the EEG and the MEG in relation to other rapidly advancing functional imaging modalities such as PET, SPECT, and functional MRI (fMRI), and in terms of the recognized research, medical, and personnel evaluation needs for advanced brain imaging. Medical areas where these and other advanced technologies will undoubtedly be utilized include the diagnosis and treatment of diseases of the brain such as epilepsy, Alzheimer's, and schizophrenia; the monitoring and facilitation of recovery of function from head trauma and stroke, and the quantitative assessment of the effect on the brain of toxins and other bioenvironmental hazards. Non-medical applications of these techniques include a furthering of our understanding of the factors that are limiting the development and full utilization of human intelligence, particularly in recognition of the increasing demands that are being placed on the mental capacities of people who live and work in our modern, post-industrial society.

A strong consensus emerged from the workshop that, because of their common electrophysiological source, the EEG and MEG share many features and should be viewed as being complementary methods, both of which will continue to play vital roles in quantitative human neurophysiology because of their unique capabilities for real-time imaging of neuronal activity with millisecond response. There is a great potential for further development of the sensitivity and specificity of these techniques because of continuing increases in the capabilities of computer software, hardware, and visualization technology. These provide, for the first time, the means to process, analyze, and interpret the data from large-scale sensor arrays now being developed. Since fMRI, PET, SPECT, EEG and MEG each have their strengths and weaknesses, and since no single modality can provide complete, real time, functional information throughout the brain, the modalities complement each other and synergistic advances can be expected from their integration.

II. The Controversy

Some controversy recently arose concerning a paper which reported that EEG and MEG produce essentially equal accuracy in localizing point dipole sources represented by sets of electrodes inserted in the human brain (Cohen 1990). This conclusion was countered by criticism that the study was based on obsolete technologies and inadequate procedures (Hari *et al.* 1991, Williamson 1991). The controversy attracted general scientific interest as a news story (Crease 1991; Tepley and Barkley 1991).

Several conferences and symposia have subsequently discussed the topic. The brief report from the European Concerted Action on Biomagnetism (Anogianakis *et al.* 1992) summarized a number of practical differences between the EEG and the MEG, and, in the context of localized sources that can be adequately modeled by a single dipole, delineated the minimum requirements for a satisfactory *in vivo* comparison of the ability to localize dipoles with the EEG and the MEG. The report recognized that more research must be performed before the relative merits of the two methods could be firmly established. However, the approach taken in that report is somewhat restrictive, in that it addresses neither the intrinsic limitations of the dipole model, nor substantive questions regarding the stability and noise-sensitivity of EEG and MEG inverse models.

In a published report of a special symposium at the 1991 meeting of the International Society of Brain Topography, the session chairman Richard Coppola (1991) stated his view that "MEG has to some extent been tauted in regard to this localization ability, so that criticism of this ability seems particularly damaging. EEG, on the other hand, has been held to be particularly limited in localization capability. As far as this part of the controversy it appears that we mainly have regression to the mean, MEG may not be a[s] good as expected and EEG turns out better than previously thought." He then went on to indicate that the real potential of both the EEG and the MEG is to reveal the millisecond-to-millisecond dynamics of neural connections. The present workshop was intended to further resolve and go beyond this controversy to discuss more basic scientific issues. In this report from that workshop, we attempt to describe the EEG and MEG from the broader perspective of the multitude of imaging modalities used to study the brain, and to discuss a variety of technical points that must be kept in mind when applying and comparing the EEG and the MEG. We do not attempt to review the latest research findings for either technique.

III. Historical Perspective

To appreciate the relative capabilities of EEG and MEG, it is helpful to consider their recent history. Prior to the introduction of computerized tomography (CT) in the 1960's and magnetic resonance imaging (MRI) in the 1980's, there were few techniques for the non-invasive study of brain anatomy, and only the EEG allowed non-invasive study of brain electrophysiology. In the mid-1980's there was a rapid advance in MEG instrumentation and research as a result of the formation of a critical mass of physical scientists and commercial firms who, for the most part, had not previously been involved with measuring brain function. In part, the impetus for developing MEG instrumentation was provided jointly by the physicists and engineers who, after having developed Superconducting QUantum Interference Device (SQUID) magnetometers primarily for basic research interests, were searching for medical and commercially-sound applications for their new technology, and by neuroscientists who were looking for new methods to study brain function. Having a strong physics orientation, the MEG community focused on characterizing the neural sources of the MEG, which required measuring the fields at many scalp locations. In contrast, during the 1980's the vast majority of electroencephalographers were neurologists who performed routine clinical examinations using 16 or 19 channel recordings and strip chart interpretation procedures that were adequate for the intended purpose and which thus had not substantially changed for several decades. The pressures of clinical duties, the lack of the required technical background, engineering staff and funding generally prevented the clinical EEG community from making any substantive improvements to their instrumentation. Commercial firms added microprocessors to clinical instruments but there were no radical technological advances in clinical EEG instruments. Although computerized topographic mapping was commercially developed in the 1980's, it did not obviate the need for examination of waveform morphology of the EEG traces, and had little impact on clinical practice. Additionally, measurements of evoked potential peak amplitude and latency were routinely used as simple indices of dysfunction, an application which did not require extensive measurement of their spatial features or neural origins. Much of the cognitive research at the time was oriented towards studies of the time course of the evoked potential at a few scalp locations, rather than the spatial dependence of the potential distribution over the entire scalp.

Consequently, there was little impetus to extend the capabilities of the EEG towards more detailed spatial mapping. The net result of the difference in culture between the young, quantitatively-oriented MEG community with its emphasis on neural generator models, and the more established, phenomenologically- and clinically-oriented EEG and psychophysiology communities was the comparison of spatially-detailed MEG measurements with ordinary EEGs and evoked potentials. Of course, the EEG was the loser of this "contest". The continued development of the MEG was motivated in part by the fact that the MEG was used to obtain research results that had not yet been found with the EEG, possibly because the vast majority of EEG practitioners were not interested in developing the level of technical or mathematical sophistication that had already been brought to bear on the MEG. Eventually, EEG researchers rediscovered that if measurements were made at more locations, the EEG could also be effectively used for dipole source modeling, and the controversy inevitably ensued.

Meanwhile, magnetic resonance imaging (MRI), Positron Emission Tomography (PET), and Single Photon Emission Computer Tomography (SPECT) techniques had been extended to allow the study of brain function and provided impressive three-dimensional images of the brain and certain aspects of its activity. As a result there are now multiple modalities competing for both research funds and potential clinical income. Vocal proponents of each modality have been known to denigrate other methods as being technically inferior or unnecessarily costly. Few investigators use multiple modalities, and objective comparisons have been slow to appear.

IV. Focus of the Workshop

At the outset of the AFOSR workshop, the organizers set a constructive tone by noting that the principals in the controversy had made their points a sufficient number of times, and that further argument without new data was pointless. Instead, the goal of the workshop was to develop a detailed assessment of the future directions for both the EEG and the MEG, and to assess the significance of ongoing theoretical and experimental developments pertinent to each technique in light of the other high-technology approaches for studying the brain. The topics discussed included the theoretical and practical aspects of the MEG and EEG, inverse problems, multimodality integration, clinical considerations and applications, perception and cognition, and the future. Rather than present a chronological account of the workshop, it is more useful to synthesize what was learned into a critical assessment of the EEG and MEG.

<u>Comparison with other techniques.</u>

The EEG and the MEG are the only techniques that offer millisecond response to brain events, in comparison to the 40 second response and several millimeter resolution offered by oxygen 15 PET. Recent advances in fMRI techniques permit 1-2 mm spatial resolution and several second time resolution of cerebral blood volume. There is currently a very rapid development of functional MRI techniques that allow measurement of changes in blood volume and other vascular-related phenomena throughout the whole head. While an fMRI image can be obtained in as short a time as 50 ms, the temporal resolution is limited by the much longer time constant for blood diffusion, approximately 2 seconds or more.

Enthusiasm about the high temporal resolution of EEG and MEG relative to other imaging modalities is tempered by the fact that there is no need to solve an ill-conditioned inverse problem in the case of PET, SPECT and fMRI, even though each of these techniques involve detailed mathematical calculations with their own inherent restrictions. PET and SPECT can image a wide variety of radioactively-labelled substances administered to the brain, and PET, SPECT, and fMRI can all image vascular events, none of which are possible with either EEG or MEG. Undoubtedly, PET and SPECT will find continued utilization in imaging neurochemistry and following the kinetics of receptor uptake over periods ranging up to hours.

With regard to cost, none of these advanced techniques is inexpensive, either in terms of hardware or staff. Of all of the techniques considered, the EEG is by far the least expensive, followed by SPECT, MEG, functional MRI, and finally PET. Given this larger perspective, the issue for the remainder of this report is to understand the strengths and weaknesses of both the EEG and MEG.

Advances in MEG and EEG Instrumentation and Measurement Techniques.

Novel MEG and EEG recording technologies currently under development will each markedly reduce the amount of time needed to obtain spatially detailed recordings over the whole head. The first full-scalp 122 channel MEG system is presently coming on line (Ahonen *et al.*, in press), and the Ministry of International Trade and Industry (MITI) in Japan has initiated a ten-company industrial collaboration to develop a 200 channel system at the new Superconducting Sensor Laboratory. Such multichannel systems obviate the need to make separate recordings at a number of sites, and are expected to reduce recording time by more than a factor of five over current commercial 37 channel systems. Moreover, signal quality will improve by more than a factor of 3 because the current limitation is imposed by "brain noise". That is, the magnetic field from adjacent areas of the brain are much stronger than instrument noise, so that when this activity can be taken into account by comprehensive simultaneous sampling of the field pattern everywhere across the scalp, the net noise level will be markedly reduced. The fixed geometric arrangement of the sensors will simplify mathematical analysis of the signals, but will lead to some loss in signal quality if the head is too small to fill the detector and closely couple to each SQUID sensor. The ability to record from all channels simultaneously will represent a major advance in the ability to map spontaneous events that cannot be reconstructed from serial measurements.

Several advances in EEG instrumentation that should simplify potential mapping were reported at the workshop. These include a 128-channel EEG Geodesic Electrode Net which can be applied in about ten to fifteen minutes (Tucker, public communication), and a 32-channel EEG recording hat with active electrodes that allows rapid setup for recordings (less than 5 minutes) without any preparation of the scalp (Gevins, DuRousseau and Libove 1991). Such systems would offer the community many of the advantages claimed by proponents of the multichannel MEG.

Undoubtedly, further technical advances should be expected for both the EEG and MEG, particularly when used in combination with each other or with other imaging techniques such as MRI. Already, the EEG and/or MEG are being integrated with individual MRI slices and three-dimensional MRI images for both research (Gevins 1987; Gevins 1989; Williamson *et al.* 1991) and clinical studies (Galen *et al.*, in press). With the availability of commercial software packages for image analysis and registration, it will be increasingly easy for more investigators to compare and integrate data from several modalities.

An often-stated merit of the MEG is that it represents a reference-free recording of the magnetic field at a single location, whereas the EEG is a measurement of a potential difference between two electrodes, one of which is generally at a fixed reference location. There have been many studies that demonstrate that EEG waveforms are sensitive to the location of the reference electrode, and, as a result, individual investigators have their own preference for reference electrode configurations, which include the potential obtained by linking both ears and the potential computed by averaging across all electrodes. The situation is complicated by the fact that commonly the reference potential is not neutral because an electrode on which it is based may have its own electric activity. For example, reference electrodes on the ear are close to the auditory cortex. If a reference electrode is placed on the body, the recordings may be subject to increased noise and muscle artifact.

The requirement for a reference electrode can be overcome by computing the surface Laplacian, performed, in its simplest form, by subtracting from a given recording one-fourth of the voltage signal recorded at each of the four surrounding electrodes to evaluate the $\partial^2V/\partial x^2$

$+ \partial^2V/\partial y^2$. The resulting Laplacian EEG maps are substantially sharper than the original EEG potential maps, for they reveal the pattern where volume current emerges from the cortex and passes through the skull into the scalp, and where it returns to the interior.

Such a presentation may be helpful in suggesting by visual inspection the locations of underlying sources. However, the sharper pattern does not in itself imply that a more accurate inverse solution for the sources can be obtained. It has been shown using a volume conductor model for activity from a single axon that the computation of a spatial derivative of the extracellular potential, corresponding to filtering out the low spatial frequencies, will sharpen the potential pattern but will also make it more difficult to perform the inverse calculation of determining the actual source configuration from the potential data (Roth and Wikswo 1985). The trade-off is between the advantages of the sharpened potential maps and the elimination of reference electrode effects, and the disadvantages of reduced sensitivity to deep sources, uncertainties in scalp and skull conductivities, the inability to compute the full Laplacian at the edges of the electrode array, and the possibility of increased instability in the inverse calculation. A more fruitful approach to spatially sharpening the EEG explicitly corrects the blurring due to conduction through the skull and other tissues (Gevins *et al.* 1991; Le and Gevins, in pres A similar Laplacian approach can be applied to the MEG, providing a sharpened pattern by either mathematical subtractions or by using planar gradiometers that measure field differences at adjacent locations on the scalp, but this will also be subject to many of the same limitations as the EEG Laplacian.

<u>The EEG and MEG Inverse Problems</u>.

Once a map of the electric or magnetic field over the surface of the scalp has been recorded, an investigator can apply pattern recognition techniques and knowledge of the location of each electrode to interpret the underlying event, as has been done in clinical EEG for decades. Alternatively, a mathematical model of the scalp-recorded EEG can be used to obtain more detailed information about the spatial location of the source (Kavanagh 1972). One of the great successes in this approach was the early MEG studies that showed how a clear magnetic field pattern recorded on the scalp could be correlated, by means of a very simple mathematical model with focal, dipolar current sources located in underlying cortical fissures (Williamson and Kaufman 1981).

Were the head and brain perfect concentric spheres, the EEG would be able to detect both radial and tangential dipoles, but the MEG, being insensitive to radial dipoles, would be able to discriminate between two hypothesized sources, one of which had a tangential component and the other of which did not (Hari *et al.* 1984; Wood *et al.* 1985). However, since the skull and brain do not form perfectly concentric homogenous shells, the selectivity of the MEG is somewhat compromised, and dipoles oriented normal to the skull may contribute appreciably. Although not physiologically realistic, point dipole models may prove to be useful in certain clinical applications. For example, magnetic location of the somatosensory strip in three dimensions can help guide surgical planning for removal of tumors that have displaced the strip from its normal locus (Galen *et al.*, in press).

In determining dipoles, there are practical differences between MEG and EEG. To a first approximation, the MEG recorded above the scalp is determined primarily by the configuration and strength of the current sources within the brain and not by the electrical properties of the intervening media. This is a result of biological tissue being transparent to magnetic fie[illegible] while being capable of distorting electric fields.

In a more accurate treatment of the MEG, the distortions in the currents within the brain, skull, and scalp, as compared to those flowing in an ideal, spherical skull, will also produce magnetic fields, but these fields are typically only a fraction of the magnetic field that comes directly from the bioelectric sources within the brain. For example, an MEG inverse model applied to frontal sources was shown to require knowledge only of the brain shape, whereas corresponding accuracy could be obtained for the EEG only with a model that included the geometry and conductivity of not only the brain but also the skull and scalp (Hämäläinen *et al.* 1989; Meijis and Peters 1987; Meijis *et al.* 1989). It is standard practice in EEG dipole analysis to take inhomogeneities into account through the use of multi-shell head models (Fender 1987).

The Limitations of the Dipole Model. Much of the MEG research and most of the ongoing controversy regarding the EEG and MEG has centered on the current dipole model for brain activity. While this model may be appropriate for simple sensory stimuli, there are important examples where it may be inadequate. For example, the cortical surface associated with an ictal or interictal epileptic spike can be as large as several tens of square centimeters and might better be described by an extended area than by a point dipole. Also, even simple mental tasks involve widely distributed neural networks. An interesting difficulty arises when a simple dipole model is applied to explain fields from such an extended source. If the density of dipoles within the layer is constant, and the dipoles are everywhere oriented normal to the layer, the source is termed a uniform double layer. For such sources, the electric and magnetic fields will be determined primarily by the shape and location of the boundary of the double layer, and the detailed geometry of the layer within the boundary will affect neither signal (Wikswo 1983). A single dipole fit for either EEG or MEG data will have a location and components that correspond to the center of mass and projected areas of the rim of the extended double layer.

In actuality, the spatial distribution of active current sources will be non-uniform, so the electric and magnetic fields will also be affected by the detailed shape of the curved surface within the boundary. The major practical problem with dipole modeling of extended neural sources is that the actual number of dipoles cannot be statistically determined from the data. This follows from the fact that many different source configurations can produce the same EEG or MEG field pattern at the scalp.

Constrained Models. While it is not possible, in principle, to overcome the inherent limitations of EEG and MEG in terms of general three-dimensional imaging throughout the brain, there are mathematical techniques to force a solution from a potentially-unstable, ill-conditioned inverse calculation. A variety of minimum norm approaches have been utilized to obtain three-dimensional images of purported currents in the brain from MEG maps (Ioannides *et al.* 1990; Ribary *et al.* 1991; Hämäläinen and Ilmoniemi 1992), but the constraints applied to the inverse calculation may provide stable solutions of questionable physiological interpretation. Similar comments apply to the method of singular value decomposition which shows that in certain circumstances it is possible to extract localized information from a complex, widely distributed potential field (Harner and Riggio 1989; Harner 1990). There have yet to be any validations of the results obtained with such an algorithm by means of a quantitative comparison with subdural potential distributions or current source density analysis.

A potentially more realistic approach is to incorporate into the model physiological constraints that were determined by other measurement modalities, such as MRI, fMRI, PET, or SPECT. For example, a recent model assumed a configuration for the cortical surface in a fissure or sulcus and applied a constraint that the primary currents would be perpendicular to the dipole surface. It was shown that in principle it will be possible to use magnetic data to obtain a best estimate for the pattern of activity distributed across broad areas of the cerebral cortex for arbitrary configurations of activity (Wang *et al.* 1992). Models that incorporate both temporal and spatial constraints or measures of covariance may be even more powerful.

Ideally, techniques will be developed that will allow the sharpening of the EEG and the MEG with minimal use of physiologically-constrained models, since such models may introduce bias or errors if the signals were, in fact, affected by an unknown brain pathology. The surface Laplacian approach is a step in this direction, as are EEG inward continuation approaches that go further to compute the potential distribution on the dura just inside the inner surface of the skull, or even further inward if there is prior knowledge about the number, location or geometry of the sources (Gevins *et al.*, 1991 and Gevins *et al.*, in press). Similar approaches have been proposed for the MEG (Nicolas and Kouwenhoven 1989; Tan, Roth and Wikswo 1990), but have not yet been implemented. Once the inward-continued potential or magnetic field at the dura has been computed, with the associated sharpening of the map features, it is sometimes possible to review the data and ascertain whether a particular physiologically-based model would be appropriate.

<u>Testing our understanding of the EEG and MEG relationship</u>.

Although there has been much discussion of the relative abilities of the EEG and the MEG to locate a dipole, the issues, as outlined in this report, are in fact much broader. The issues include: how to treat multiple close-lying sources and extensive sources that cannot be properly modeled by a single dipole or an ensemble of two or three dipoles; how to gauge the effects of external and brain noise on inverse algorithms; how to incorporate physiological and anatomical constraints to inverse calculations, as well as the role of anisotropies in the electrical conductivity of brain tissues, and whether quantitative measurements of absolute source strength have diagnostic utility. Absolute source strengths are often deduced in MEG studies, while in EEG studies relative source strengths are computed due to lack of knowledge of tissue conductivities. The best scientifically-sound means to ascertain whether the inverse models are producing realistic results and to test the EEG/MEG relationship is to compare the models with intracerebral data from neurosurgery patients (Cohen *et al.* 1990; Balish *et al.* 1991; Sutherling and Barth 1989) or to use animal models (Barth and Di 1990; Gardner-Medwin, *et al.* 1991; Huang *et al.* 1990; Okada *et al.* 1987; Okada *et al.* 1988; Okada, in press).

Applications of EEG and MEG to Cognitive Science.

Some cognitive scientists recognize a need for more sophisticated network models and more clever experimental designs to deal with the complexities of widely distributed neural processes. An opinion was expressed that studies of event-related responses have had little impact on the development of cognitive science, because very few of them address issues of prime interest to the cognitive community. However, the use of a large array of EEG electrodes now makes it possible to determine sub-second functional associations between cortical areas characterizing working memory and other basic cognitive functions (Gevins *et al.* 1981; Gevins *et al.* 1983). Such studies demonstrate the necessity of understanding post-stimulus cognitive processing in the context of the subject's internal model for the environmental conditions and specified task (Gevins *et al.* 1987). In the past, MEG applications were also hindered by the lack of large sensor arrays, but here as well the development of arrays of 37 and 122 sensors has overcome this obstacle. But even without instruments with many sensors, it is possible to conduct useful research by locating the position of a neural source and then placing the instrument to obtain the strongest signal. This advantage was exploited in a recent study of habituation in the primary and association auditory cortices in which evidence was obtained that the neuronal activation trace has a markedly shorter lifetime in the primary cortex than in the association cortex (Lu *et al.* 1992) and correlates with the lifetime of echoic memory (Lu *et al.*, in press). While the new technologies make it possible to monitor many EEG and MEG channels, in practice the knowledge gained from studies in cognition is less dependent upon the sophistication of the hardware used by the investigator than upon the skill of the investigator in devising an appropriate paradigm and unravelling the resulting data!

V. Conclusion

It is unlikely that the differential sensitivities of the MEG and EEG to radial versus tangential sources is of sufficient importance alone to significantly influence the relative ranking and utility of the EEG and the MEG. The main advantages of the MEG follow from the fact that MEG signals are not highly distorted by conduction through the skull between sensors and scalp. The main disadvantages are that the subject can not move during a recording and the technology is at present expensive and requires a massive magnetically-shielded room. While magnetic contamination poses serious difficulties, the MEG can also be used to detect non-invasively DC shifts associated with phenomena ranging from spreading depression to head injury (Barkley *et al.* 1991; Gardner-Medwin *et al.* 1991).

Conversely, the main advantage of the EEG is that it is inexpensive and can be recorded in a natural environment. The EEG is also better suited for studies of the brainstem because the sources are deep, making them difficult to detect with the MEG. The major disadvantage of the EEG is that detailed information about the external and internal geometry of a subject's head is needed to correct for spatial blur from conduction through the skull. Also, it is necessary to establish good electrical contact with the skull, but this is less of a problem with high impedance active electrodes (Gevins, DuRousseau and Libove 1991).

Coppola (1991) points out that at present a multichannel, clinical MEG system costs about 25 times more than an EEG system with a similar number of channels, and the potential benefit to a patient must justify this cost differential. However, he notes that the issue of cost is different for a research environment, where the additional information gained may justify the cost, particularly if there is no other way to obtain this information. Substantial costs for technicians to apply 128 EEG electrodes by traditional techniques may well be cut dramatically by the advent of high impedance amplifiers and simpler procedures for securing electrodes (Gevins, DuRousseau and Libove 1991).

A large number of device- and modeling-oriented research groups worldwide have invested heavily in developing the MEG as a quantitative technique for assessing brain function. Unfortunately, because of the constraints imposed by accepted clinical practice and the historical bias regarding the limitations of the EEG, there has been substantially less effort directed towards pressing EEG recording and analysis techniques to their theoretical limits. Cross-fertilization of the efforts between the two communities should lead to substantive improvements in both techniques.

When both the MEG and the EEG, as well as their users, are at the same level of technical and physiological sophistication, it will undoubtedly be possible to obtain additional returns on the collective intellectual investments by fully merging the two techniques to obtain even more accurate and stable source reconstructions, as was done using single-channel SQUIDs several years ago (Wood *et al.* 1985).

Both the MEG and the EEG are expected to undergo further development in the next few years. Extension of the capabilities of the EEG is within easy reach, particularly once techniques are devised for automatic placement of up to 256 electrodes and effective artifact recognition. The future of the MEG lies with the large, whole-scalp multichannel SQUID systems. Advanced noise rejection, signal processing, and source-characterization algorithms will benefit both approaches. In response to the need to improve the diagnosis and treatment of neurologic and psychiatric diseases, rapid development of several other technologies that measure complementary aspects of brain anatomy and function is taking place concomitantly, especially including PET and SPECT, and fMRI for structure and function. Since all of these imaging modalities have their strengths and weaknesses, and since no single modality can provide complete, real time, functional information throughout the brain, the modalities are truly complementary.

Moreover, synergistic advances can be expected from the integration of the EEG and MEG with the other modalities. Intercomparison of data obtained by EEG and MEG with complimentary studies using invasive electrodes in patients, or PET, SPECT, and fMRI in patients and normal subjects will provide important validations across modalities. Animal models and tissue preparations will provide additional validation at a more detailed and better controlled level.

As Hans Berger had hoped, human neurophysiology can serve as a "window on the mind" by performing real-time imaging of mental functions of the brain. This Holy Grail of our field is much closer to realization than was thought possible even a few years ago.

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WORKSHOP PROGRAM

MONDAY, MAY 18

18:30 -- 19:30	Mixer
19:30 -- 20:30	Buffet Dinner
20:30	Welcome and Introduction -- Weinstock and Fregly

TUESDAY, MAY 19

08:30 Topic 1: Theoretical and Practical Aspects of MEG and EEG -- Chair: Nunez

08:30 Wikswo	Fundamental factors that affect the EEG and MEG -- information content, silent sources, spatial resolution, inward continuation, and such
09:15 Williamson	Advantages of MEG
09:35 Gevins	Advantages of EEG
09:55 Coffee	
10:10 Sutherling	Practical factors that affect the EEG and MEG -- subject preparation time, subject immobilization, artifacts, signal to noise ratio of sensors, instrument cost, technical support

10:30 Panel: Barth, Tepley, Okada, Regan, Tucker plus Topic 1 speakers

12:00 Lunch and Mid-Day Break

15:30 Topic 2: Inverse Problems -- Chair: Wikswo

15:30 Nunez.	Single and multiple dipole models and inward continuation
16:00 Hamalainen	New possibilities and challenges in source analysis through full-scalp magnetic coverage
16:30 Williamson	Unique estimates for distributed cortical activity

17:00 Panel: Gevins, Robinson, Okada plus Topic 2 speakers

18:00 Coffee

18:15 Topic 3: Multimodality Integration -- Chair: Williamson

18:15 Coppola	Integration of EEG/MEG with MRI, PET and SPECT
18:45 Wood	Integration of MRI and EEG/MEG

19:15 Panel: Gevins, Lauterbur, Sutherling plus Topic 3 speakers

20:00 Dinner

WEDNESDAY, MAY 20

08:30 Topic 4: Clinical Considerations and Applications -- Chairs: Harner and Ebersole

08:30 Ebersole	Practical application of source localization in partial epilepsy
09:00 Harner	Clinical applications of quantitative electrophysiology
09:30 Sato	Comparison of MEG and EEG in localizing epileptic foci
10:00 Coffee	
10:15 Gallen	Clinical applications of magnetic source imaging

10:45 Panel: Barkley, Barth, Sutherling plus Topic 4 Speakers

12:00 Lunch and Mid-Day Break

16:00 Topic 5: Perception, Cognition, and Action -- Chair: Wilson

16:00 Regan	MEG and EEG in research on parallel processing in vision
16:45 Gevins	Dynamic cortical networks of mental models and simple tasks
17:30 Coffee	
17:45 Kaufman	Differential activity of cortex: EEG, MEG, and PET as complementary modalities
18:30 Cooper	How brain data help a cognitive scientist

19:15 Panel: Nakamura, Tangney, Tucker, Wood plus Topic 5 Speakers

20:15 Banquet

THURSDAY, MAY 21

08:30 Topic 6: The Future -- Chair: Weinstock

08:30 Tangney	Goals and Perspectives of the Air Force
08:50 Lawrence	Goals and Perspectives of the Army
09:10 Nakamura	Goals and Perspectives of the NIMH

09:30 Discussion and Questions

10:00 Coffee

10:15 Copolla	The Future of SPECT and PET
10:35 Lauterbur	The Future of Functional MRI
10:55 Gevins	The Future of EEG
11:15 Williamson	The Future of MEG

11:35 General Discussion

12:00 Closing Remarks -- Weinstock and Fregly

12:15 Lunch

SCIENTIFIC INTERESTS OF ATTENDEES

Allard: Developing basic research programs in neuro-cognitive science for the Cognitive Science Program of the Office of Naval Research. Our goal is to develop better theories of human intelligence and information-processing capacities by understanding the multiple neural substrates of cognition. We have a special focus on high-level cognitive processes in humans and computational modeling of human cognitive architectures. Navy payoffs include improved prediction of individual differences in cognitive performance, improved human factors design, and improved instructional technologies. Current program supports work in visual cognition and memory systems. Personal research in behavioral neuroscience (human neuropsychology of speech and auditory perception and animal neurophysiology of use-dependent changes in sensory-motor representations).

Barkley: Gregory L. Barkley MD is the Medical Director of the Henry Ford Hospital-Oakland University Neuromagnetism Laboratory. After graduating from Michigan State University College of Human Medicine in 1981, he did his neurology residency and fellowship in clinical neurophysiology and epilepsy at Henry Ford Hospital. He is board certified by the American Board of Psychiatry and Neurology and the American Board of Clinical Neurophysiology. He is a senior staff physician in the Department of Neurology at Henry Ford Hospital and is the Director of the EEG Laboratories and the Director of the Adult Epilepsy Clinic. His research interests include the study of slowly varying neurophysiologic phenomena by DC-MEG and DC-ECoG such as spreading depression, anoxia, and epilepsy. He has also focused upon the use of DC-MEG in migraine and techniques for DC-MEG in humans. He is actively involved in clinical trials of experimental antiepileptic drugs.

Barth: My research is concerned with the electrophysiology of sensory information processing in animal and man, and pathological changes in the neurocircuitry of sensation produced by epilepsy. This work involves high resolution mapping of neuromagnetic and neuroelectric fields produced by populations of neurons, and numerical methods for discriminating interactions between brain regions in space and in time.

Cooper: Professor and Chair of Psychology Department, Columbia University Research in the area of visual cognition and perception. Specific interests in the mental representation of visual objects and events.

Coppola: Dr. Richard Coppola is chief of the Neuro-imaging Unit in the Clinical Brain Disorders Branch, National Institute of Mental Health Intramural Research Program located at the NIMH Neurosciences Center at St. Elizabeths, Washington, D.C. His particular research interests have involved developing and applying functional brain imaging for the study of neuropsychiatric disorders as well as gaining a better understanding of the neurophysiological substrate of normal cognition and sensory processing. The methods presently in use include

Single Photon Emission Computed Tomography and quantitative electrophysiological mapping techniques as well as Positron Emission Tomography and Magnetic Resonance Imaging.

Ebersole: I am actively engaged in developing quantitative EEG (voltage topography) and dipole modeling of interictal potentials and ictal rhythms as new clinical tools in the evaluation of focal epilepsy. Since many of the patients we have studied ultimately require intracerebral and subdural electrodes prior to surgical therapy, we are in the fortunate position of being able to verify our predictions about the character of the cerebral generators of the signals measured at the scalp. Our goal is to be able to characterize cerebral epileptogenic sources sufficiently well by quantitative EEG analysis that the number of patients who need to undergo intracranial monitoring is minimized. I believe we have the most active clinical program of this type in the country, and I would be glad to share our experiences, data, and thoughts with the other participants. Since our data are new, not well known, and already quite extensive, I would like to be able to present them in some detail. Having also just returned from a sabbatical leave at the MEG Center in Albuquerque, I have an appreciation for the relative strengths and weaknesses of both EEG and MEG techniques, as they apply to clinical research efforts.

Fregly: Research in cognition and electromagnetic brain activity; brain and behavior; cognitive neuroscience.

Gevins: For the past 20 years I have been developing analytic methods, software systems and experimental paradigms for measuring the neuroelectric basis of human cognition. My approach is based on measuring the activity of rapidly shifting cortical networks as subjects perform simple but difficult cognitive tasks. Our current measurement technology includes 124-channel EEG recordings, three-dimensional finite element brain and head models derived form each subject's magnetic resonance images, correction of EEG recordings for spatial distortion due to transmission through the skull and other tissues, and computation of time-dependent correlations between evoked potentials recorded from different sites.

Hämäläinen: I am putting together the software for a whole-head MEG system. My current interest include multidipole and continuous-distribution source modelling, realistic conductor models, and MEG-MRI integration.

Harner: EEG analysis of epileptic force using singular value decomposition of sources, waves, spikes, & frequencies.

Lauterbur: Magnetic resonance imaging and spectroscopy of brain structure and function.

Lawrence: My relevant interest is to monitor developments in this area on behalf of Army Research Institute.

Regan: 1. Visual psychophysics (motion, spatial vision, depth, binocular vision, colour)
2. Clinic psychophysics (multiple sclerosis, parkinson's disease, amblyopia, cataract, glaucoma)
3. Auditory psychophysics
4. MEG & EP studies of sensory systems; vision in aviation, space & sport

Robinson: Considerable emphasis has been placed on the use of MEG and EEG to localize components of an averaged evoked response. However, only a small fraction of the human brain is directly involved in either primary sensory or primary motor activities. I would like to discuss the role of MEG and EEG in localizing spontaneous (unaveraged) brain activity, and its potential contribution to cognitive as well as clinical science. Materials I have available for discussion include MEG measurements of epileptic discharges, single trial (unaveraged) evoked response, video of current image movies, and computer simulations.

Sato: Application of EEG and MEG in clinical epilepsy research to localize an epileptogenic zone.

Sutherling: The overall scientific interest and activities of the Reed-UCLA Neuromagnetism laboratory are to investigate the capabilities of dipole models applied to the extracranial magnetic and electric fields for localization and quantification of electrically active human cortex with specific applications to non-invasive presurgical localization of human partial seizures for focal excisional surgery. As a natural extension of this research, investigation of human somatosensory cortex has been performed. Comparisons are made between the non-invasive measures and invasive intracranial measures including chronically placed subdural grid electrodes and depth electrodes, with additional anatomical studies.

Tangney: Sensory, motor and cognitive processing in biological systems. Behavioral, neural and computational approaches to these issues.

Tepley: Norman Tepley, Professor of Physics at Oakland University and Scientific Director, Henry Ford Hospital-Oakland University Neuromagnetism Laboratory received his Ph.D. in physics from M.I.T. in 1963. His research centered on low temperature physics until 1976, when funded by the Michigan Heart Association, he began to study biomagnetism. During 1980 through 1982 he organized and initiated a non-radiological Ph.D. program in Medical Physics at Oakland University and assembled a consortium of Detroit area hospitals to participate in the research aspects of the program. In 1986, in collaboration with K.M.A. Welch, M.D., chairman of Neurology at Henry Ford Hospital, he began plans for a Neuromagnetism Laboratory. That laboratory was completed in May 1988. Since that time his research interests have focused on very slowly varying neurophysiologic phenomena which might best be studied non-invasively with DC-MEG. In addition he has worked on a variety of new techniques for the analysis of MEG and EEG data.

Tucker: My scientific interests include neuropsychological models of emotion and psychopathology, emotional influences on attention and cognition, developmental neuroscience, quantitative analysis of scalp electrophysiology.

Weinberg: Neurophysiology of information processing.

Wikswo: My biomagnetic research has been directed towards using simple electrophysiological preparations and mathematical models to understand the relationship between the electric and magnetic fields associated with propagating action potentials. We have studied isolated nerves, skeletal muscle, smooth muscle, and one- and two-dimensional cardiac tissue. We have developed high resolution torodial and SQUID magnetometers to enable us to image magnetic fields and currents.

Williamson: The direction of my research is to elucidate the relationships between macroscopic neuronal activity of the human brain and perceptual and cognitive performance. The approach is to relate magnetic source imaging (MSI) \- which establishes quantitative measures of neuronal activity at identifiable locations within the brain \- and behavioral measures on the same subjects. To this end, our laboratory at NYU has been developing neuromagnetic techniques over a period of nearly 20 years with a goal of providing a unique, quantitative characterization of the distribution of neuronal activity within the brain.

Wilson: My scientific interests are to better understand human performance using physiological measures. In particular I am interested in human cognitive workload. I use EEG and MEG measures to gain insight into how the brain processes information when task difficulty is manipulated. I am becoming increasingly interested in multiple task environments in both the laboratory and "real world".

EVALUATION OF WORKSHOP

What is the most important concert or fact that you learned at this workshop?

[1] The material was very new to me, so virtually everything was a learning experience. (I was quite surprised at how sophisticated EEG has become!)

[2] There is no single best general way to image electromagnetic brain activity given the differential goals and requirements of basic and applied research and clinical situations.

[3] It might be useful to provide an inward continuation of $\vec{B}$ up to the brain's surface.

[4] That we need measures of local control activation, with high spatio-temporal resolution, and that correlate with other measures of local cortical metabolism and/or neuronal activity, to be used especially for studies of cognition.

[5] No response to this question.

[6] The EEG/MEG localization problem is under better control because fewer things are being done wrong and more of the available information, experimental and theoretical is being used. However, general solutions are still not available, and probably never will be. Worse, there is no way to tell a good approximate solution from a bad one.

[7] Advances in functional imaging.

[8] That there is a convergence of the capabilities of MEG and EEG. Also that the scale of the way we look at brain (point dipole <--> whole brain) can change the manner of extracting information.

[9] Theoretical: Green's function, spatial resolution for multiple sources of MEG (power spatial Fourier Transform).
Technical: whole head, geodesic EEG electrode cap.

[10] New thoughts concerning possible collaborations with cognitive scientists.

[11] MEG data is being used to determine surgical procedures.

[12] Interdisciplinary research particularly concerning cognition is a higher priority than I thought.

[13] The workshop was a very informative conference on EEG and MEG, particularly because EEGers, MEGers, and other neuroscientists met, discussed, and exchanged information face to face. The underlying concept of not dwelling on a discussion of whether one method is superior to another, I think, led to the success of this workshop.

What is the most pressing scientific question that you leave with?

[1] How can these methods be used to understand the nature of cognition? (Despite my remarks, I have become convinced that this is a realistic and desirable goal).

[2] How can mechanism of brain functioning be best elucidated?

[3] Fusion of discrete and continuous source modelling approached.

[4] How to fully interpret EEG & MEG data.

[5] How can we best exploit the potentially synergistic relation between MEG/EEG and functional MRI?

[6] How to identify the most pressing scientific question. Perhaps it is how to integrate good spatial localization with good temporal resolution, so that EEG & MEG will often need to be localized only well enough to reveal which MRI/PET etc. spot is associated with which response in a sequence.

[7] Lack of formulation specific linking hypotheses to be tested (structure-function).

[8] Combination (or feasibility, thereof) of MEG/EEG and other neuro-"imaging" modalities is needed to advance clinical and basic scientific research on the brain.

[9] Technical scientific questions: (1) Is it feasible to image human cortical regions with errors: center of mass 1-2 mm, area ~/0%, temporal asychrony 1 msec? (2) Is MEG >=< EEG?
Brain scientific question: What is functional anatomy of somatosensory perception?

[10] Need for well-defined standards against which various new modelling schemes can be tested.

[11] What level of analysis is best for cognitive work? Sources, areas, patterns of sources/areas? Technology for ECG/MEG is doing well, is time to study cognitive effects where sharp responses one finds with sensory studies do not see to occur.

[12] Modelling sources of activity must be carefully done using a variety of techniques in order to arrive at unambiguous answers.
Whether some of the officials who review our proposals.

[13] Complementarity between EEG and MEG was well recognized by all participants, but the application of this concept to epilepsy research is not yet conceptualized. Thus, the combination of EEG and MEG needs to be established in terms of its practical utility. This undertaking may have to be delegated to those who have both EEG and MEG capability. The news on Neuromag-122 was welcome. One group appeared to claim that MEG is a clinically useful tool, even though there is no solid evidence of such usefulness of the methodology. The application of the current density method to epilepsy research must be explored.

What points should the summary report emphasize?

[1] Complementarity of approaches.
Notion of combining methods (EEG & MEG with PET, MRI).
Idea the cognition task analysis should make contact with EEG/MEG research.

[2] What are the current capabilities and limitations of available brain imaging techniques and how can they be improved to impact future imaging capabilities for improving human intellectual functional in normal and abnormal work and health situations.

[3] MEG & EEG are both useful tools for studying brain function. MEG modelling is more straightforward. Combined use is an important but largely unexplored territory.

[4] Complexity of sources.
Need for more sensors/unit space.
Need for regular communication, workshops etc. in the EEG/MEG analysis community.

[5] Complementarity.

[6] Integration of EEG/MEG/MRI etc. to address well-defined fields of unique, basic or clinical. This does not have to be the "NNL" but can be done by encouraging funding agencies to ask for it and to promise money for well-concerned joint projects.

[8] That there is a vast area of research to be done in marrying electrophysiology to cognitive science. Without cross fertilization, MEG/EEG will stagnate!

[9] How to best improve spatiotemporal imaging of dynamic brain function.

[10] 1.The need for better communication between the clinical researchers and the basic neuroscience researchers.
2. Questions concerning the utility of EEG and MEG for basic and clinical research require much more research (and money) to answer.

[11] EEG-MEG complement one another and should be used together.

[12] 1. All researchers are limited by the high costs of multichannel MEG and EEG recordings which limits our ability to do the simultaneous multichannel MEG/EEG recordings that most seem to feel are needed to resolve issues raised in the meeting. Thus more money is needed.
2. A number of attempts have been proposed to replace the ECD but none have been conclusively proven superior.

[13] MEG is an excellent experimental tool, but it is not a clinical tool. EEG has made tremendous advances within the past decade, but needs refinement and further exploration in different areas of application, particularly of the (inward continuation) method of Gevins. This method needs to be explored to do the same thing in deeper structures of the brain, as well as superficially. The complementary nature of EEG and MEG needs to be emphasized, but the continuous exploration of EEG is as important as their relationship.

What points should the summary report not emphasize?

[1] (I don't really understand this question...)

[2] Controversies of any kind

[3] Cohen's notorious paper as a starting point.

[4] EEG vs. MEG.

[5] The dipole argument.

[6] The NNL
Specific hardware
EEG vs MEG

[8] None - be frank!

[9] Unsupported, anecdotal findings.
Findings from black-boxes which cannot be replicated/validated or understood by common scientist or common clinician.

[10] 1. EEG versus MEG.
2. The bad rap that the current dipole received from many participants.

[11] 1. That there is a better feud between EEG and MEG couples.
2. That ECG or MEG is absolutely the best measure for everything.

[12] Dr. Gevins' criticism of the equivalent current dipole which differs greatly from the opinions spoken by the rest of the group.

[13] Any statements implying that one method is better than the other should be avoided.

How might the workshop organization, food, or facilities have been improved?

[1] It was excellent.

[2] The addition of two or three more "Card Carrying" cognitive psychologists.

[3] The weather could have been better on Tuesday & Wednesday!

[4] Not easily improved!

[5] Fine as it was.

[6] Juice for breakfast
Avoid the uncomfortable Horizon Room

More sunshine and warmth

[7] Fine.

[8] Encourage more interactive panel discussions. Perhaps an agreed-to list of questions to be solved or debated might help!

[9] More time for discussion (perhaps shorter midday break).

[10] 1. Somewhat more time for one-on-one conversation.
2. Otherwise - very good job! Thank you.

[11] Include a group picture to avoid numerous flashes, clicks and whiring(sic) noises during the meeting!! Facilities, food, etc. were great - well done, timer was good idea.

[12] 1. The breakfasts had too much fat - sausages, bacon, hash brown etc., I would emphasize juice, fruits, cereals etc. Also better wines with dinners would be nice.
2. The meeting was well organized and the time keeper did as good job of keeping on track. Discussions were fruitful.

[13] The workshop was well organized and the participants were well fed.

WHAT NEW CHIPS OFF OLD BLOCKS?

When researchers stop counting to ten,
And the patients start smiling again,
And all brain functions known,
Thanks new seeds here were sewn,
Will John Wikswo at last say, "Amen"?

Will the brain models left to compose
Prompt such poetry rather than prose,
And when all s done and said,
Will a brain that's well read
Make it clear that we smell like a rose?

Will the cognitive types jeer or cheer,
Or be doomed to still cry in their beer,
When techniques we behold
Are more bold and best told
Without dipoles provoking their fear?

Will John Tangney feel much more at ease
At less things that have caused him to sneeze,
And will Weinstock be pleased
That news skids were well greased
Or, like some, still be wailing "Aw geez"?

And will Alan and Sam, Lloyd and Chris
Always tell us their research can't miss,
If our faith is ne'er lost,
At whatever the cost,
For our mutual sharing of bliss?

And will Sutherling/Sato/Okada
Be satisfied soon, as they oughta,
If Paul Lauterbur's stuff
Shows them more than enough,
And all clinical types join with "Uh huh"?

-Al Fregly, Prog. Mgr., AFOSR (Ret.)

REPORT OF EXPENDITURES

Salaries & Benefits:	
Office Clerical Wages	$1,507.88
Total Salaries & Wages	$1,507.88
FICA	115.36
Health Insurance	196.65
Group Life Insurance	5.45
Disability Insurance	7.11
Other Fringes	0.00
Total Benefits	$324.57
Total Salaries & Benefits	$1,832.45
General Supplies:	
Duplication	0.00
Postage	188.53
Office Supplies	798.46
Lab Supplies	59.00
Telephone - Long Distance	0.00
Meetings Expense	6,173.55
Rental of Equipment	1.55
Total General Supplies	$7,221.09
Travel Expense:	
Travel Faculty	4,579.98
Travel Students	852.45
Travel Other	2,466.03
Total Travel Expense	$7,898.46
Total Supplies & Travel	$15,119.55
Total Expenses	$16,952.00
Grant Total	$16,952.00
Total Unspent Balance	$0.00